REMARKS

Applicants have responded to all outstanding objections/rejections as discussed herein hereinbelow.

Applicants have amended the claims for purposes of expediting prosecution and for placing the application in condition of allowance. No new matter has been added by this amendment.

Examiner's Interview Summary

The applicants wish to thank the examiner for the useful and professional interview and, in particular, the extra efforts the examiner evidently undertook to prepare for the interview.

The primary substantive issue discussed was the 103 rejection. In particular, the examiner and the undersigned discussed the particular structural features of the presently amended claims in their relation to the disclosure of the Pennell *et al.* patent.

The examiner suggested that the applicants add a cross-reference to related applications section to the specification (which the applicants do herein).

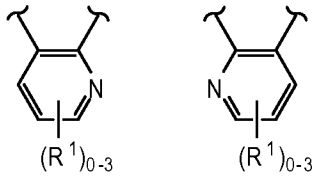
The examiner also noted that the PTO's bibliographic data sheet indicates that there is some discrepancy between the PTO's data with respect to the PCT application of which the present application is the US national phase and the data the applicants supplied. The examiner could not identify the discrepancy, and neither can the applicants. The PCT application number and filing date reported in the Application Data Sheet submitted on national phase filing appears to be identical the PTO's records. The applicants respectfully request clarification.

The examiner also requested that the claims be limited to the elected group. In response, the applicants have canceled the withdrawn claims. The pending claims are directed to compounds in which Ar is pyridine not further substituted, which is the subject matter of the elected group.

Rejections under 35 U.S.C. § 112, second paragraph

(1) The Office rejected claims 1, 5-24, 27, 28 and 43 under 35 U.S.C. § 112, second paragraph, alleging that the phrase "–Y-L-Z in an ortho position to each other" os not clear as to what group–Y-L-Z is ortho to. In response, Applicants have amended the definition of Ar to clearly define this ortho relationship of –Y-L-Z and X as follows:

Ar is selected from the following formulae



wherein Ar is substituted with –X and -Y-L-Z, in an ortho relationship to each other."

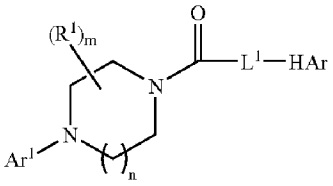
Support for this amendment can be found in original claim 1 as filed. This rejection has been rendered moot by this amendment. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

(2) The Office rejected claim 5 and its dependent claims for being dependent on Canceled claim 4. In response, Applicants have amended claim 5 to be dependent on claim 1, thereby rendering this rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejections under 35 U.S.C. § 103(a)

The Office has rejected claims 1, 5-24, 27, 28, 30-36. 39. 40 and 43 under 35 U.S.C. § 103(a), alleging that these claims are unpatentable over Pennell et al., U.S. 7,449,576. Applicants respectfully traverse.

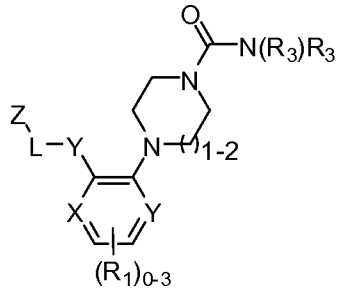
Pennell et al. discloses compounds of the following general structure:



(I)

wherein n is 1 or 2 (col. 9, ll. 28-29), L^1 "represents a linking group having from one to three main chain atoms selected from the group consisting of C, N, O and S and being optionally substituted with from one to three substituents" (col. 10, ll. 61-64), HAr is an optionally substituted heteroaryl (co. 10, l. 1), and Ar^1 is an optionally substituted aryl or heteroaryl group (col. 9. Ll. 35-36). Pennell *et al.* teaches these compounds as chemokine inhibitors (CCR1 receptor antagonists, in particular).

The presently amended claims are directed to Tie-2 kinase of modulators of the following general structure:



where one of X and Y is N and the other is –CH-, and, in certain embodiments having the closest structural similarity to Pennell *et al.*, (a) both R^3's together with the nitrogen to which they are attached form a 5- to 7-heterocyclyl ring (such ring defined in the specification to include heteroaryl), or (b) one R^3 is H and the other is an optionally substituted lower heterocyclylalkyl.

In order to arrive at the presently claimed compounds, one of ordinary skill in the art would have to pick and choose from myriad combinations and permutations of the various moieties broadly encompassed with the genus disclosed by Pennell without guidance directing them towards the presently claimed compounds and without an expectation that such compounds would be Tie-2 modulators. For example, Pennell neither exemplifies nor otherwise suggests the following combinations of features found in the presently claimed compounds as being preferred:

1. the urea structure on the piperidine ring (i.e., >N-C(O)-N(R^3)R^3);
2. a structure comprising a cyclic substituent on Ar^1 that corresponds to –Y-L-Z (which comprises a cyclic moiety); and
3. the ortho relationship between the piperidine moiety and the –Y-L-Z substituent.

And more than not guiding one of ordinary skill in the art towards the presently claimed compounds, in certain instances Pennell et al. directs the ordinary artisan away from them. For example, rather than L^1 of Pennell being N to give the urea structure found in the presently claimed compounds, Pennell teaches that L^1 is preferably selected from –CH_2-, -CH_2CH_2-, -CH_2OCH_2-and -CH_2NHCH_2- (col. 5, ll. 18-21). Thus, among the large group of possible L^1 linkers, Pennell teaches towards those that result in an amide functionality rather than the urea functionality of the presently claimed compounds.

In addition, the substituents of all the Ar^1 moieties as exemplified in the compounds disclosed in Fig. 5, the synthetic examples, and the Table beginning in col. 38 of Pennell et al. are all rather small and simple (e.g., halo, methyl, methoxy, dimethylaminosulfonyl) whereas the corresponding substituent of the pyridine moiety of the present claims, –Y-L-Z, comprises a cyclic moiety. There is nothing in Pennell et al. guiding the ordinary artisan to substituents such as –Y-L-Z alone or in combination with the other features of the presently claimed compounds.

Without guidance directing one of ordinary skill in the art towards the presently claimed compounds and without it being reasonably predictable that such compounds would possess the property of by an Tie-2 kinase modulator, as discovered by the present inventors, the claims cannot be obvious. Accordingly, the applicants respectfully request reconsideration and withdrawal of this rejection.

No fees are believed to be due in order to process this document and any paper attached. Should the U.S. Patent Office determine that an extension of time and/or other relief is required at this time, the Commissioner is authorized to charge the cost of such relief and/or fees to deposit account no. 13-2490.

If it is believed that a teleconference will advance prosecution, the examiner is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

Date: July 26, 2010

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